Déjà vu and the entorhinal cortex: dissociating recollective from familiarity disruptions in a single case patient

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Abstract

Past research has demonstrated a relationship between déjà vu and the entorhinal cortex in patients with wider medial temporal lobe damage. The aim of the present research was to investigate this crucial link in a patient (MR) with a selective lesion to the left lateral entorhinal cortex to provide a more direct exploration of this relationship. Two experiments investigated the experiences of déjà vécu (using the IDEA questionnaire) and déjà vu (using an adapted DRM paradigm) in MR and a set of matched controls. The results demonstrated that MR had quantitatively more and qualitatively richer recollective experiences of déjà vécu. In addition, under laboratory-based déjà vu conditions designed to elicit both false recollection (critical lures) and false familiarity (weakly-associated lures), MR only revealed greater memory impairments for the latter. The present results are therefore the first to demonstrate a direct relationship between the entorhinal cortex and the experience of both déjà vu and déjà vécu. They furthermore suggest that the entorhinal cortex is involved in both weakly-associative false memory as well as strongly-associative memory under conditions that promote familiarity-based processing.

Key words: Entorhinal cortex, familiarity, recollection, déjà vu

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Introduction

The mistaken feeling of familiarity associated with encountering something known to be novel is a relatively oft-reported experience within the general population (for reviews see Brown, 2003; Illman, Butler, Souchay & Moulin, 2011). Known as déjà vu, this experience can arise for both people and places and critically the feeling of familiarity accompanying déjà vu is knowingly detected as a false memory. Hence the perceiver is aware that this feeling of familiarity is wrong, which importantly distinguishes this false memory from other types of false familiarity experiences such as false positives when the perceiver deems the sense of familiarity to be an actual true memory. In being able to detect that the source of the memory is incorrect (i.e., that the item is in fact novel despite the sense of having encountered it before), déjà vu experiences are also distinguishable from those experiences arising under Recognition Without Awareness paradigms. Within this paradigm, experimental manipulations such as speed of presentation and use of word fragments, enable participants to distinguish true from false memories in the absence of being able to identify the items per se (Cleary & Green, 2004, 2005; Craik, Rose & Gopie, 2015; Voss, Baym & Paller, 2008).

In trying to understand the nature behind the déjà vu phenomenon, and given the difficulty in creating such experiences within laboratory settings, research has often focused on those clinical populations that appear to report elevated déjà vu during seizure activity. Temporal lobe epilepsy (TLE) patients are typically divided into those that do (TLE+) and do not (TLE−), experience déjà vu experiences, prior to and during epileptic seizures (Gloor, 1990; Martin et al., 2012). Those TLE patients that do report déjà vu, experience the same sort of déjà vu experiences reported by healthy individuals, in being aware of having a false sense of familiarity. However, during seizure activity, these patients can also experience having visually intense flashbacks and hallucinations, the experiential richness of which clearly differs from simply a lower level sense of familiarity (Gloor, 1990; Martin et al., 2012). This observed distinction between the different qualitative experiences that can accompany déjà vu experiences as well as the need to provide a sound theoretical account of the causes of this phenomenon,

has provoked research into addressing key issues such as distinctions within the déjà vu experience, familiarity versus recollective contributions to déjà vu and the role of distinct areas within the medial temporal lobes to this experience.

Given the difference in qualitative richness observed in the déjà vu experiences of TLE patients, an important distinction has been made between the terms déjà vu and déjà vécu, which are seen as lying on a continuum. Déjà vu, literally meaning “already seen”, reflects a brief disruption to low level familiarity in that the experience itself is not accompanied by any rich contextual detail such as visual illusion or emotion (Illman et al., 2012). Whereas déjà vécu, meaning “already lived” involves a contextually-richer and longer experience involving mental time travel and hence more reflective of recollection-based disruption and therefore unlike déjà vu, is more likely to involve a range of medial temporal lobe structures (Illman et al., 2012).

Importantly the distinction between experiences of déjà vu and déjà vécu is one which TLE patients are aware of. Using the Inventory of Déjà-vu Experiences Assessment (IDEA), research has demonstrated that TLE patients were clearly aware of and could differentiate between healthy (déjà vu) and seizure-related (déjà vécu) experiences (Adachi, et al., 2010). Furthermore, in a single case TLE patient study, O’Connor and Moulin (2008) demonstrated that, whilst not being able to prevent persistent déjà vu experiences from taking place, by attempting to stop these arising prior to seizures, the patient could differentiate between healthy and seizure-based déjà vu. Taken together this research does not support the contention that the causes of déjà vu in patients is due to simple memory errors. Being able to recognise that the sense of familiarity experienced for something novel is incorrect is the critical distinction between experiences of déjà vu as opposed to a false positive when such a distinction cannot be made. The critical question is whether the déjà vu experiences in TLE patients are selectively linked to activity in restricted brain areas or whether such disruption is more widely evidenced across the medial temporal lobes.

According to dual process accounts of recognition memory (Aggleton and Brown; 1999; Montaldi & Mayes, 2010), within the medial temporal lobes, whilst the hippocampal system elicits the recollective process, the perirhinal system is responsible for the process of familiarity. Whilst evidence linking the hippocampal system purely to recollective processes in both healthy and brain-damaged patients has been robust (Brandt, Gardiner, Baddeley, Vargha-Khadem & Mishkin, 2009; Diana, Yonelinas, and Ranganath, 2007; Mayes, Holdstock, Isaac, Montaldi, Grigor, Gummer et al., 2004; Yonelinas, 2002), evidence linking the perirhinal system to the process of familiarity has been more sparse (De Vanssay-Maigne, Noulhiane, Devauchelle, Rodrigo, Baudoin-Chial, Meder, et al., 2011). Nevertheless, several notable patient cases do exist. One case involves a TLE+ patient who following a left unilateral lesionectomy for intractable epilepsy which removed a large part of her left perirhinal system (perirhinal and entorhinal cortices) whilst leaving her hippocampal system intact, demonstrated a selective impairment for familiarity (Bowles, Crupi, Mirsattari, Pigott, Parrent, Pruessner, et al., 2007; Martin, Bowles, Mirsattari, & Köhler, 2011). A second more recent case involving an even more unique TLE+ patient with a selective lesion to the left lateral entorhinal cortex also demonstrated an impairment in familiarity in the context of normal recollection (Brandt, Eysenck, Kragh-Nielsen, & von Oertzen, 2016; James, Norbury, von Oertzen, Huppertz, & Brandt, 2018). The rarity of such patients makes the link between the perirhinal system and the process of familiarity more difficult to test, however these two cases support the contention of a selective relationship between the perirhinal system, and more specifically the entorhinal cortex and the process of familiarity.

Given the evidence linking the perirhinal system to the process of familiarity, evidence should also exist linking these areas and familiarity to déjà vu experiences. Work in TLE+ patients has revealed that such a relationship is indeed robust. This has demonstrated that within the medial temporal lobes, the entorhinal cortex is the area that is most metabolically altered in such patients (Guedj, Aubert, McGonigal, Mundler and Bartolomei, 2010). In addition, déjà vu has been found to arise significantly

more when stimulating the entorhinal cortex compared to the amygdala or hippocampus (Bartolomei, Barbeau, Gavaret, Guye, McGonigal, Régis, et al., 2004). Furthermore, only TLE+ as opposed to TLE - patients were found to have a selective impairment in familiarity as opposed to generic familiarity and recollective impairments (Martin et al., 2012), although such a behavioural distinction has been observed in one case patient who is non-epileptic/seizure-free (Edelstyn, Grange, Ellis & Mayes, 2016). The above research therefore highlights an important relationship between déjà vu, the entorhinal cortex and the process of familiarity. Importantly, O'Connor and Moulin (2013) demonstrated that no such relationship appeared to exist in healthy individuals as they found that neither recollection nor familiarity correlated with déjà vu propensity. This therefore suggests that the relationship between déjà vu, the entorhinal cortex and the process of familiarity is unique to TLE+ patients. Such a unique relationship might be due to TLE+ patients experiencing over stimulation to the entorhinal cortex during seizures that are over and beyond that experienced by both TLE- patients as well as the non-TLE population when experiencing déjà vu. However, this relationship has only been tested in patients with damage beyond the entorhinal cortex and therefore the precise contribution of this area to déjà vu elicitation remains unexplored. The aim of the present research is to therefore investigate the relationship between déjà vu and familiarity in a patient with a selective lesion to the left lateral entorhinal cortex.

Experiment 1: IDEA (Inventory for Déjà Vu Experiences Assessment)

The present experiment used the IDEA to measure quantitative and qualitative déjà vu experiences in a patient with a selective lesion to the left lateral entorhinal cortex in comparison to a set of matched control participants. This questionnaire has reliably been used on TLE+ patients demonstrating that they can differentiate between healthy (déjà vu) and seizure-related déjà vécu (Adachi et al., 2010) but the nature of the questions suggests they tap more strongly into addressing the latter type of experience. Given conversations with the patient in which she described in vivid detail both the déjà vu and seizure-related déjà vécu experiences she had, we predicted that she would report quantitatively more, and

qualitatively richer déjà vécu experiences in comparison to controls, reflecting presumed wider medial temporal lobe activity disruption during her seizure activity (Bartolomei et al 2004).

Methods

Participants

The University of Roehampton Ethics Committee and the National Research Ethics Service approved the experimental procedures for all present experiments reported prior to the start of the research. Furthermore, all procedures were carried out with written informed consent of the participants as well as the patient with all being informed they could withdraw from the research at any time and without having to give a reason. MR and seven healthy female control participants, all of whom were native English speakers and had fluent written and spoken English took part in the present research which was conducted at the University of Roehampton. The present set of control participants were matched to patient MR using a modified t-test developed for use in single case studies with small control samples (Crawford & Howell, 1998). No differences between MR and the controls were found in terms of age (MR = 50, controls = 49) nor on performance in the National Adult Reading Test (MR = 103, controls = 108.28), $p > .05$. In addition, further neuropsychological profiling was carried out using the WASI (Wechsler Abbreviated Scale of Intelligence), the Doors and Peoples Test and the WMS (Wechsler Memory Scale). Crawford's t-test revealed no significant differences between MR and the controls on any of these measures $p > .05$, (see Table 1 for scores). Participants were given monetary compensation for their travel and participation.

Clinical profile of MR

A full clinical profile and 3T MRI scans for MR are provided in a previous paper (see Brandt et al., 2016). MR is a right-handed female patient who started to suffer from complex partial seizures at the age of 36 which included partial seizures with déjà vu and complex partial seizures with or without déjà-vu. When MR was 42, a small cavernoma in her left anterior parahippocampal gyrus was diagnosed on MRI.

When MR was 48 she was referred for pre-surgical assessment and 3T MRI then confirmed that the lesion she incurred was restricted to the left anterior parahippocampal gyrus and more recently has been more specifically located to the lateral left entorhinal cortex (Brandt et al., 2016; James et al, 2018). Given MR's clinical symptoms, the size and pathology of her MRI lesion and her EEG results, she presents as a well-defined case of left symptomatic temporomesial epilepsy due to a small cavernoma in the left entorhinal cortex (See Figure 1).

Materials and Procedure

The IDEA consists of 23 questions assessing the quantitative and qualitative aspects of the déjà vu experiences a person can have and is split into two parts. The first part is a general section assessing a person's experience of déjà vu (e.g., "Have you ever had the feeling of having experienced a sensation or situation before in exactly the same way when in fact you are experiencing it for the first time"?) and answers are quantified ranging from "never" to "more frequently" with an option to respond "don't know". The second part of the IDEA consists of 14 questions that assess the qualitative aspects of a person's déjà vu experiences (e.g., "While you have this feeling of *recognition'* can you remember exactly where and when you had the same experience or feeling before"?). The IDEA has demonstrated good reliability and validity (Sno, Schalken, de Jonghe & Koeter, 1994) and is therefore a useful tool in comparing the déjà vu experiences in TLE patients to the wider population. The IDEA is self-administered and participants in the present experiment typically took about 10 minutes to complete it.

Results

The results were analysed using Crawford's modified t-test. For Part 1 of the questionnaire, answers were scored such that the higher the frequency of the particular déjà vu experience the answer was addressing, the higher the score attributed to that question. For example, to the question "Have you ever had the feeling that it seems as if everything around is not real, as if it is not really happening?" the answer "never" scored 0, the answer "very infrequently" scored 1, the answer "sometimes" scored 2, the

answer “often” scored 3 and finally the answer “more frequently/at least weekly” scored 4. Total scores were then added up for each participant and revealed that MR (M = 3.63) had significantly more experiences of déjà vu in comparison to the controls (M = 2.34, SD = .47, range = 1.89 – 3.14), t(6) = 2.56, p = .02.

For Part 2 of the questionnaire, 5 of the 14 questions were quantifiable Yes/No questions. For example, to the question “Have you ever had this feeling of ‘recognition’ in one or more of the following ways?” participants could respond either Yes or No to 10 different statements (e.g., in a certain place, when meeting someone). The total “Yes” responses for each of these questions were then added up to give each participant one total score. This demonstrated that MR (M = 20) scored marginally higher than the controls (M = 10.42, SD = 5.12, range = 4 - 17), t(6) = 1.75, p = .06. The remaining 9 questions revealed that the main qualitative déjà vu differences emerging between the controls and MR, was in terms of the last time déjà vu occurred (MR = 1-5 years ago, controls = 1-12 months), duration of déjà vu (MR = 3-5 minutes, controls = few seconds), full or partial relation of déjà vu to situation (MR = full, controls = some part), whether déjà vu occurs at a given time (MR = mornings, controls = no/don’t know) and finally whether déjà vu feels as if everything around is not real (MR = yes, totally unreal, controls = never/don’t know).

One of the key qualitative differences between MR and the controls was to the question about the feeling of recognition happening in a number of ways (i.e., in a place, in a situation, during an activity, at a certain event, when meeting someone, whilst telling someone something, whilst listening to something, whilst having a thought, whilst reading). MR answered yes to all 9 possible ways (the controls answered mostly no to all 9 ways). In addition, she responded “yes” to experiencing this recognition “in some other way” and wrote: “When having a seizure, I drift off into a dream world state where everybody and any activities seem familiar, while everything around me, ‘reality’, becomes unreal-unrecognised.” This quote highlights that although the feeling of déjà-vecu is all encompassing for MR, she is still aware

this is based on a false sense of recognition in referring to this experience as a “dream world” and reality becoming unreal and unrecognisable. The results of the IDEA questionnaire therefore demonstrate that in comparison to the controls, MR has significantly more experiences of déjà vu. More importantly, they reveal that these experiences are qualitatively different to those of the controls, in being significantly more encompassing, vividly rich and lasting significantly longer. These experiences are therefore consistent with richer recollective disruption associated with the experience of déjà vécu (Illman et al., 2012). However, the present results do not support previous research showing less, rather than more déjà vu in TLE+ patients (Adachi et al., 2010). This discrepancy is likely due to a key neurological difference between MR and the patients used in the Adachi et al (2010) research. Specifically, their patients had differentiating lesions to medial temporal lobe and hemispheric regions whereas MR has a selective lesion to the (left) lateral entorhinal cortex which is the area most heavily implicated in déjà-vu (Bartolomei et al., 2004; Guedj et al., 2010). This further reinforces the importance of using single case patients with selective lesions in order to more fully establish localisation of function.

Given MR’s clear evidence of enhanced déjà vécu arising from seizure-related recollective disruption, the question remains whether under non-seizure conditions, she demonstrates greater experiences of déjà vu that are typically based on a sense of familiarity rather than recollection. This question was addressed in the following experiment that attempted to elicit both enhanced false recollective and false familiarity recognition within an experimental setting.

Experiment 2: DRM

The aim of the current experiment was to attempt to elicit déjà vu experiences experimentally by adapting a false memory paradigm and to see whether such disruptions gave rise to increased familiarity-based déjà vu experiences in MR. This premise was tested using the Deese-Roediger-McDermott (1995) (DRM) paradigm. In this paradigm, participants are presented with a list of words that are all related to a critical lure word that is not presented. Roediger and McDermott (1995) found that participants falsely

recall and recognise the critical lure word around 40% of the time, which is much higher than would be expected for a lure item (known as the DRM effect). This effect is believed to be due to each item on the list generating increasing associative strength to the critical non-presented word which then triggers (false) memory for that item. Indeed, research has demonstrated that the greater the associative strength of the presented words, the more likely the critical lure will not only be recognised, but be recognised on the basis of rich episodic recollection (Deese, 1959; Roediger & McDermott, 1995; Roediger, Watson, McDermott & Gallo, 2001).

Given the above finding, one possibility is that words with a weaker associative strength to the critical lure word, whilst still eliciting false recognition, might be less likely to do so on the basis of strong recollective processes. That is, the weaker associative strength of these items is less likely to generate rich episodic contextual cues at retrieval and therefore more likely to be accompanied by familiarity processes, the precise process that is implicated in eliciting the experience of déjà vu (Illman et al., 2012). Using DRM lists that generated the highest critical lure recognition, past research has shown that manipulating whether non-critical lures are related or not to the list presented, leads to an 18% false recognition rate for related lures (high familiarity, low novelty condition, Urquhart & O'Connor, 2014). These related lures were taken from the bottom of each DRM list and therefore represented the weakest associative strength items which are more likely to be falsely recognised on the basis of familiarity rather than recollective processes (Roediger et al., 2001). As such, the use of these items was deemed ideal in the present experiment in an attempt to elicit familiarity disruption.

Hence, within the present DRM experiment, several key predictions were made. Firstly, that MR would demonstrate normal overall recall, recognition and recollection processes given her spared hippocampal system and past research showing these processes to be comparable between her and controls (Brandt et al., 2016; James et al., 2018). Secondly, that MR was expected to have similar levels of critical lure recognition as the controls given that past research has shown that recognition of these

lures is based on strong recollective processes (Roediger & McDermott, 1995) that are normal in MR. Finally, and most importantly, that MR should demonstrate higher false recognition for weakly associated lures. This prediction was made on the basis that such items would be more likely to disrupt familiarity processes that appear to be the key to MR's selective familiarity impairment (Brandt et al., 2016).

Methods

Participants

The control participants were the same as in Experiment 1. The University of Roehampton Ethics Committee and the National Research Ethics Service approved the experimental procedures for all present experiments reported prior to the start of the research and all procedures were carried out with written informed consent of the participants as well as the patient.

Materials and Procedure

Participants firstly took part in a recall test in which they were serially presented with 6 DRM lists taken from Deese and McDermott (1995). These 6 lists (Anger, Chair, Sweet, Doctor, Sleep and Needle) were selected on the basis of being those most likely to elicit false memory of the critical lure (Deese & McDermott, 1995). The procedures closely modelled those in the original paper. Each list contained the first 12 most strongly associated words of the DRM list (i.e., highest associative strength to the critical lure word). Each word was presented for 1500 msec with a 1000 ISI using Psyscope. The serial order of the words in these lists is such that the first word is the one most strongly related to the critical lure word with decreasing strength going down the list. Following presentation of the first list, participants received an immediate recall test in which they were given 2 minutes to recall as many words as possible and in any order. They were then presented with the second list and the same procedure ensued. After the 6th and final list was presented, participants received a 5 minute distractor task in which they were given sums to complete.

This recall test was then followed by a computer recognition test consisting of 60 words, 30 old (5 target words from each list) + 30 new words (6 critical lures + 12 words taken from non-presented DRM lists [4 positive, 4 neutral and 4 negative] + 12 weakly associated words). The 12 weakly related words consisted of the 13th and 14th word from each of the 6 DRM lists. Hence, they were selected on the basis of being non-presented category members of presented DRM lists (e.g., yawn, cake, peace) that are the most weakly associated words in those lists to the critical lure word. Words were randomly presented to participants and for each word, participants were required to decide whether it had been previously studied (old) or not (new). Following a decision that the word was old, participants were further required to decide whether their recognition was based on contextual recall (remember response), recognition in the absence of contextual recall (know response) or simply a guess. (Please insert Figure 2 here).

Results

Recall

The results were analysed using Crawford's modified t-test (2-tailed) and revealed no significant differences between MR ($\underline{M}$ = .53) and the controls ($\underline{M}$ = .64, SD = .17, range = .33 - .92) in correct recall $\underline{t}(6) = -.60$, $\underline{p} = .56$. Nor were any differences found between MR (M = 1) and the controls ($\underline{M}$ = .60, $\underline{SD}$ = .30, range = 0 - .83) in terms of critical lure recall $\underline{t}(6) = 1.24$, $\underline{p} = .25$. Differences however were found in terms of unrelated false recall MR (M = 6) and the controls ($\underline{M}$ = 1.71, $\underline{SD}$ = 1.38, range = 0 - 4), $\underline{t}(6) = 2.98$, $\underline{p} = .02$.

Recognition Memory

Proportion of hits, critical lures and both weakly-associated and non-associated lures for remember and know responses were submitted to Crawford's modified t-test. As the proportion of guess responses was too low and has also been shown not to reflect any memory discriminability (Gardiner, Ramponi & Richardson-Klavehn, 1998), no analyses were performed on these data. Correct (hits) and incorrect

(critical lures, weakly and non-associated lures) for remember and know responses were firstly analysed separately, both due to previous work demonstrating that MR's impairment appears to reflect an inability to reject distractors rather than an inability to accept targets (Brandt et al., 2016; and so that any possible performance dissociation in MR between strength of semantic association within incorrect recognition (i.e., lures) could be identified. Secondly the results were also analysed following previous statistical methods on single case patients (Brandt et al., 2016, Bowles et al., 2007) using the correction of independence model whereby remember response accuracy (i.e., hits-false alarms) were taken as an indication of Recollection and with the correction of independence being applied to know responses [Familiarity = know/(1-remember)] to gain an estimate of familiarity (Yonelinas & Jacoby, 1995). Finally recognition memory was quantified using the discriminability index d' based on signal detection theory (Snodgrass & Corwin, 1988) and response criterion was calculated using the criterion location measure (C). Significance levels are given as 2-tailed unless specified.

With regards to correct hits, no differences emerged between MR and the controls in terms of remember responses $t(6) = -.38$, $p = .71$. However MR scored significantly higher correct know responses $t(6) = 3.74$, $p = .01$ (please see Table 2 for all treatment means and ranges of scores). The analyses on critical lures revealed no significant differences between MR and the controls either in remember responses $t(6) = .79$, $p = .45$ or in know responses $t(6) = 1.40$, $p = .21$.

In terms of non-associated lures, no differences emerged in remember responses $t(6) = .31$, $p = .76$ and no analyses were performed on know responses as the controls did not make any of these type of responses. However critically, in terms of weakly-associated lures, significant differences emerged between MR and the controls both in remember $t(6) = 1.98$, $p = .04$ as well as in know responses $t(6) = 2.18$, $p = .03$ demonstrating that regardless of memorial quality, MR made significantly more errors in rejecting weakly-associated lures. In fact, whereas the controls' recognition of non-associated to weakly-associated lures went up by 5%, MR's error rate went up by 17%. The d' analysis on remember responses

revealed MR (M = 1.05) performed similarly to controls (M = 1.86, SD = .94), t(6) = -.80, p = .45. Nor were there any difference in terms of response criterion (MR, M = .08, controls, M = .22) t(6) = -.46, p = .65. The d' analysis on know responses revealed MR (M = .51) performed similarly to controls (M = .52, SD = .54), t(6) = -.01, p = .98. However MR was significantly more liberal when making these types of responses (MR, M = .87, controls, M = .1.87, SD = .24), t(6) = -3.89, p = .008. Finally, no differences emerged between MR and the controls either in recollection t(6) = -.70, p = .47 (MR: M = .42, controls: M = .64), or in familiarity, t(6) = .78, p = .46 (MR: M = .14, controls: M = .04).

These results demonstrate that under conditions that support recollective-based recognition (correct targets and non-presented strongly semantically related words; i.e. critical lures), MR performs at the same level as control participants. However, under conditions that are likely to elicit familiarity processes (i.e., weakly associated lures), she performs significantly worse than controls. Importantly, MR's normal performance under strong recollective-based conditions with impaired performance under weaker familiarity-based conditions, arose in the context of overall normal recognition memory. A full discussion of these results in relation to those of Experiment 1 are presented below.

Discussion

In trying to understand the mechanisms and brain areas involved in the process of déjà vu, previous research has demonstrated an important relationship between déjà vu, the entorhinal cortex and the process of familiarity (Illman et al., 2012). Additionally, this relationship with the process of familiarity but not recollection appears unique to TLE+ patients as opposed to both TLE− patients (Martin et al., 2012) and healthy participants (O'Connor and Moulin, 2013). However, such a relationship has only been investigated in TLE patients that have extensive medial temporal lobe damage and therefore the precise contribution of the entorhinal cortex to the process of déjà vu and déjà vécu remains unexplored. The key aim of the present research was to therefore address this issue in a unique patient with a selective lesion to the left lateral entorhinal cortex.

The results of the IDEA questionnaire demonstrated that in comparison to controls, MR had significantly more encompassing and vividly rich experiences that were directly linked to occasions prior to and during epileptic seizures. This qualitatively rich experience is more reflective of déjà vécu than déjà vu and is consistent with the recollective disruption that is evidenced during seizure-based activity in TLE+ patients and which causes wider disruption within the medial temporal lobe area (Martin et al., 2012). However, under non-seizure based laboratory conditions that give rise to déjà vu experiences, MR's main impairment was found following manipulations that were more likely to enhance false familiarity (weakly-associated lures) compared to false recollection (strongly-associated critical lures). The present research is therefore the first to demonstrate a direct relationship between the entorhinal cortex and the experience of both déjà vu and déjà vécu and supports past research showing this relationship in patients with wider medial temporal lobe damage (Bartolomei et al., 2004; Guedj et al., 2010).

At first glance, the present results suggest a differentiating role of the left entorhinal cortex in semantic associative memory. Hence whilst strong semantic associations were not affected in MR (e.g., critical lure recognition), weaker semantic associations tapped into her memory impairment preventing her from being able to differentiate true from false memories. This supports previous research showing that MR's impairment manifested itself in the false recognition of verbally-familiar distractors which were not strongly associated within the study list context (Brandt et al., 2016). However, they are not supportive with previous research demonstrating MR's impaired performance for strong semantic associations within a priming paradigm (Brandt et al., 2016). In addition, in comparison to controls, MR demonstrated both higher levels of false remember and know responses for weakly-associated lures. Furthermore, her false remember responses were higher than her false know responses. This pattern was not predicted given past research showing MR has a selective impairment in familiarity alone (Brandt et al., 2016). However, this pattern was importantly the same for controls and therefore suggests that unlike

non-associated lures (that tend to be recognised more on the basis of familiarity rather than recollection), weakly-associated lures give rise to more false recognition based on recollection than familiarity. As strongly associated lures (critical lure) are also recognised more on the basis of recollection than familiarity (Roediger & McDermott, 1995), this suggests a common pattern of enhanced false recollection for all associative non-presented items, regardless of associative strength. Despite MR showing the same pattern of remember/know responses as the controls for false recognition, she demonstrated a different response criterion for them. Critically, her know responses, but not her remember responses, were associated with a significantly more liberal response criterion (as previously found, Brandt et al., 2016) and this in itself might also explain the greater know responses she made in correct recognition.

Hence, the present results demonstrate that MR has a generic issue for weakly associated lures that is not specific to know responses that are reflective of the process of familiarity (Gardiner & Java, 1993). Furthermore, the present finding that MR demonstrates normal strongly associative memory (critical lure recognition) in light of previous research showing she has impaired strongly associative memory (priming, Brandt et al., 2016) suggests that she does not have a generic issue with strongly associated semantic verbal material. Rather, these results suggest that under conditions where experimental manipulations give rise to strong semantic associations based on the process of recollection (critical lure in the DRM paradigm; Roediger & McDermott, 1995), MR performs normally, however under conditions where experimental manipulations give rise to strong semantic associations based on familiarity (priming experiment in Brandt et al., 2016; Wang & Yonelinas, 2012), or only weaker semantic associations (weakly-associated lures), MR is impaired.

These results are supportive of dual process models of recognition memory in two critical ways. Firstly, they support the separation of recollection and familiarity within the medial temporal lobes (Aggleton & Brown, 1999). Secondly, they reflect familiarity as being a continuous process of intra-item

sensory and perceptual integrations. In other words, stronger semantic associations reflect greater integration of an event leading to higher confidence familiarity whereas weaker integration only gives rise to less confident feelings of familiarity (Yonelinas, 2002). MR's spared hippocampal system supports recollective-based processing whereas her selective left lateral entorhinal cortex lesion impairs her familiarity-based memory both for strongly (Brandt et al., 2016) and weakly-associated (present research) verbal memory.

One question that emerges is whether MR's impairment reflects a generic recognition without awareness issue, in that she is unaware that the feeling of familiarity she experiences is incorrect or rather reflects a proper déjà vu experience in that she is aware that her sense of familiarity is misplaced. The evidence strongly points to the latter. Firstly, MR demonstrated normal levels of recall, recognition and recollection in comparison to control participants. Hence her memory issue is not a generic recognition failure per se, which is further consistent with previous research on MR (Brandt et al., 2016; James et al., 2018). These results support those found by Martin et al (2012) who also found that TLE+ patients did not have a generic memory issue unlike their TLE- patients who did. Secondly, MR has indicated both in conversations and in her written description of what happens during her seizure-based déjà vécu experiences that she is fully aware that these are not based on true recognition and like previous patients can differentiate these from the normal déjà vu she experiences outside seizures (Adachi et al., 2010; O'Connor & Moulin, 2008). As the awareness that a sense of familiarity is false is the main characteristic differentiating déjà vu experiences from generic false positive recognition (Illman et al., 2012), these results strongly support the view that MR's experiences are reflective of the phenomenon of déjà vu rather than a generic false positive recognition issue. Hence the present research demonstrates that MR's lack of an overall memory deficit and her awareness of her false sense of familiarity, support the contention that her memory impairments are linked to déjà vu-specific issues when encountering familiar verbal material rather than a generic recognition without awareness problem per se (Cleary & Green, 2004; Craik et al., 2015). Furthermore, they suggest that her selective left lateral entorhinal cortex lesion

causes her to have both high level disruptions during seizures leading to déjà vécu experiences, as well as lower level disruption outside seizures (for verbally familiar material) leading to experiences of déjà vu.

In conclusion, the present research demonstrates that MR experiences both enhanced levels of déjà-vu and déjà vécu in comparison to controls which are not a generic recognition without awareness issue. Rather her enhanced déjà vécu reflect enhanced false recollective experiences which are most likely caused by wider disruption to the medial temporal lobes during seizure activity (Martin et al., 2012). Her enhanced déjà-vu under non-seizure laboratory conditions, is most likely caused by her selective lesion to the medial temporal lobe area most involved in eliciting this experience; the entorhinal cortex (Bartolomei et al, 2004). This therefore is supportive of the contention that the déjà vu phenomenon is better viewed as being on a continuum whereby déjà vu experiences reflect low level disruption based on entorhinal cortex activity whereas déjà vécu experiences reflect high level disruption to more extended medial temporal lobes areas (Illman et al., 2012). Coupled with previous research (Brandt et al., 2016), the present research, in providing a more direct investigation between the entorhinal cortex, déjà vu and the process of familiarity, demonstrates the involvement of this brain area in both weakly associated false recognition and strongly associative recognition under conditions that promote familiarity rather than recollective-based processing.

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Table 1.

Controls and MR's scores as a function of Neuropsychological Test

	MR	**Controls**
WASI	114	102.14 (14.87)
Doors and People	10	10.57 (3.99)
WMS:		
General	96	105.28 (20.81)
Auditory immediate	94	99.71 (18.99)
Visual immediate	115	101.85 (16.34)
Memory immediate	105	100.85 (19.56)
Auditory delayed	92	101.57 (15.92)
Visual delayed	109	107.14 (18.52)

Auditory recognition delayed	96	102.85 (22.51)
Working memory	105	94. 42 (13.62)

Note. Standard deviations in parentheses.

Table 2.

Proportion of hits and false alarms for MR and controls as a function of word type (Experiment 2).

Hits	**Remember**	**Know**	**Guess**	**Overall**
MR	.67	.27	0	.94
Controls	.74 (.17)	.07 (.05)	.09 (.08)	.90 (.10)
	[.40 - .90]	[.03 - .10]	[0 - .23]	[.70 – 1]
Critical Lure				
MR	.83	.17	0	1
Controls	.55 (.33)	.05 (.08)	.19 (.22)	.79 (.27)
	[0 - .83]	[0 - .17]	[0 - .17]	[.33 – 1]
Lures				
Weakly Associated				
MR	.25	.08	.08	.41
Controls	.08 (.08)	.01 (.03)	.07 (.10)	.16 (.15)
	[0 - .25]	[0 - .08]	[0 - .25]	[0 - .42]
Lures				
Non associated				

MR	0	.17	.08	.25
Controls	.01 (.03)	0	.11 (.15)	.12 (.18)
	[0 - .08]	[0 – 0]	[0 - .42]	[0 - .50]

Note. Standard deviations in parentheses. Range of control scores in brackets.

Figure 1.

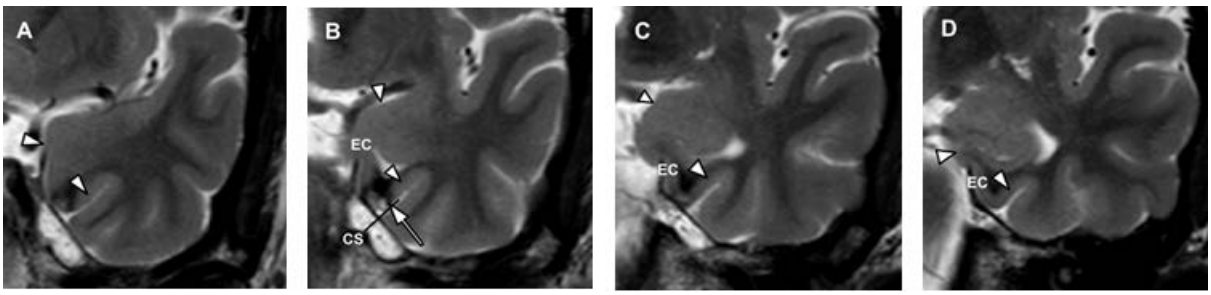
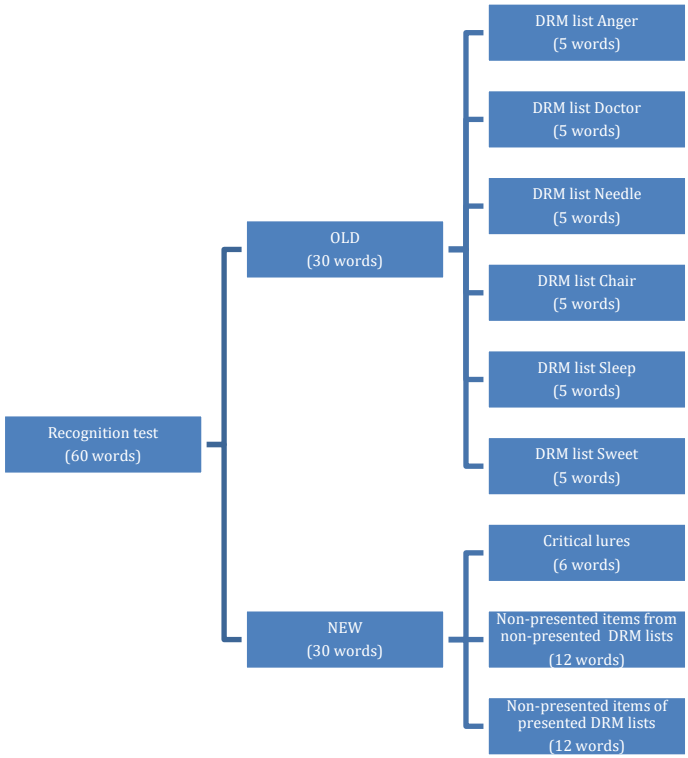


Figure 1. T2-weighted coronal imaging of MRs cavernoma (white arrow, EC = entorhinal cortex; CS = collateral sulcus). Orientation of the coronal images is perpendicular to the longitudinal axis of the hippocampus and slice thickness is 2 mm. Following previous protocol (Insausti et al 1998) this series of images shows the landmarks used to identify the hippocampal and rhinal cortical areas. It would appear that MR's cavernoma and its surrounding hemosiderin halo (surrounding susceptibility artefact = black) covers the lateral part of the left entorhinal cortex, as in Reagh & Yassa (2014).

Figure 2.


Recognition test
(60 words)
OLD
(30 words)
NEW
(30 words)
DRM list Anger
(5 words)
DRM list Doctor
(5 words)
DRM list Needle
(5 words)
DRM list Chair
(5 words)
DRM list Sleep
(5 words)
DRM list Sweet
(5 words)
Critical lures
(6 words)
Non-presented items from non-presented DRM lists
(12 words)
Non-presented items of presented DRM lists
(12 words)